RECENT ADVANCES IN THE MANAGEMENT OF THE Rh-INCOMPATIBLE PREGNANCY

*Introductory Remarks**

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THIS symposium entitled "Recent Advances in the Management of the Rh-Incompatible Pregnancy" should be exciting and instructive. I wonder if we realize how relatively recent a concept this whole Rh problem is in modern medicine.

Just for fun, I went back to one of my favorite authors, August Ritter von Reuss. (If you don't know him, you should; von Reuss was the most famous authority in the world, I suppose, on pediatrics for the newborn from about 1915 into the 1920's in Vienna, Austria. His textbook, *The Diseases of the Newborn*,[1] although it is long since out of date, is still fascinating to read.) I looked up what he had to say about erythroblastosis fetalis and the Rh problem, and I had to refer to a section in his book called "General Diseases of Obscure Aetiology." Here, after discussing the jaundice of syphilis and the jaundice of atresia of the bile duct, he writes: "There remain cases to be mentioned of severe icterus which have been described as 'habitual icterus gravis.'... The disease is associated remarkably often with meningeal signs of irritation, hyperesthesia, screaming, tonic spasms of the extremities and back muscles. In the course of the first week, it generally leads to collapse and death. . . . Relatively often, though not invariably, at the post-mortem examination yellowish discoloration of the nuclei is found . . . which is in striking contrast to the usual pale yellow diffuse colour of the rest of the nervous system. . . . The term 'habitual' icterus is used because, in some cases, it is so often repeated among children of the same parents, though healthy children are born in between or only with mild icterus."

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In another section of his book he talks about "hydrops foetus universalis." Let me quote again briefly.

". . . there are some cases of congenital oedema which are undoubtedly due to a common cause. These cases are more interesting from the clinical aspect, because they consist mostly of premature infants who are born dead or who die a few minutes after birth. . . . The most characteristic feature of the post-mortem findings is said to be an enlargement of the spleen. Histological examinations reveal the presence of well-developed areas of haematopoiesis in the liver, kidneys and spleen. The blood picture is very striking, containing numerous erythroblasts. . . . The cause of the disease is unknown; but it is not syphilis."

Thus von Reuss, in 1921.

Hydrops fetalis, icterus gravis, and anemia neonatorum, for all their Latin names, remained mysterious and supposedly separate diseases until 1932, when Drs. Louis K. Diamond, Kenneth D. Blackfan, and James A. Baty[2] concluded they were actually closely related and dependent upon some dysfunction of erythrocyte production, and they coined the term so familiar to us, "erythroblastosis fetalis."

This was in 1932. Then, in 1940, Drs. Karl Landsteiner and Alexander S. Wiener[3] discovered the Rh blood factor. A year later Philip Levine and his associates[4] suggested that erythroblastosis fetalis might result from the hemolytic action of maternal isoantibodies on the red cells of the fetus. In that same year, Levine's group, with Peter Vogel,[5] showed that 93 per cent of cases of gross erythroblastosis fetalis result from isoimmunization of an Rh-negative mother by the Rh factor in the red cells of her fetus.

Then, in 1947, Dr. Diamond and Dr. Fred H. Allen and their associates developed and popularized the exchange transfusion. This has remained our mainstay of treatment to prevent kernicterus. It cannot, however, save the stillborn infant, and only rarely can it save the hydropic infant. We still await a practical method of intrauterine therapy and, above all, we still await a means of prevention—of neutralizing the maternal antibodies or preventing their formation.

ABO incompatability is not of direct concern to the obstetrician, because these babies are born in fairly good shape. Rh incompatability, however, is not only the pediatrician's problem—of saving the baby if it does survive—but the obstetrician's problem: that of delivering to the

pediatrician a baby early enough to prevent it from dying in utero (worldwide, about 10 per cent of these babies do so); and also early enough to prevent it from dying of the disease immediately after birth (perinatal mortality in this disease is, I believe, about 20 per cent). But the obstetrician must not deliver the baby to the pediatrician so early as to cause death from prematurity. We badly need guidelines for the necessity of and the timing of induction.

Rh incompatibility is not really an exotic disease: one of every 200 babies born in the United States suffers from it. We have pretty well conquered kernicterus with properly performed exchange transfusions. We have learned to save some babies from otherwise fatal anemia at birth by means of packed-cell transfusions. But the problem of the stillborn infant with this disease and the problem of the fatally hydropic infant remain, and these problems are still largely unsolved. And the problem of the difficult and sometimes dangerous exchange transfusion with its 1 to 5 per cent mortality remains.

We have come a long way since 1921, when von Reuss knew only that the disease was not caused by syphilis, but we still have much to learn about saving these babies.

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